DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I (claims 121-146 and 189-192) and the species of SEQ ID NOs: 1 and 6 (representing a VH and VL combination found in a TSHR 1 monoclonal antibody), in the reply filed on 23 October 2007 is acknowledged. Applicant's amendments to the claims are also acknowledged.

The traversal is on the grounds that independent claims 121 and 189 have been amended to include a limitation that the binding partner has a characteristic of patient serum TSH autoantibodies (Remarks, p. 18 of 19, third paragraph). Applicant argues that these amendments render the amended claims novel over the cited reference "in which there is no mention of autoantibodies as found in patient serum" (Remarks, p. 18 of 19, third paragraph). Applicant argues that "while autoantibodies are mentioned in the cited reference (for example on [p]age 3, where they are indicated as a cause in Grave's disease) there is no indication that the antibodies made in the reference have the characteristics of autoantibodies" (Remarks, p. 18 of 19, fourth paragraph). Applicant argues that claim 121 as amended is novel over the art and that there is no remaining basis for the assertion of lack of unity (Remarks, p. 18 of 19, fifth paragraph).

Applicant elects Group I, other than claim 192, but recites the election as a group of claims consisting of claims "146-182 and 189-190" (Remarks, p. 18 of 18, third paragraph). It is unclear whether Applicant's recitation of claims 146-182 and 189-190 is a typographical error or whether Applicant is requesting that claims 146-182 and 189-190 be examined as Group I. Claims 121-146 and 189-192 were the original Group I.

Applicant requests reconsideration of the separation of the claims in Group II (claims 147-155) because "[a]s a general rule, PCT Unity of Invention Rules do not separate nucleotide and corresponding amino acid sequences in different inventions" (Remarks, p. 18 of 19, fifth paragraph). Applicant argues that the restriction requirement should be withdrawn (Remarks, p. 19 of 19, first paragraph). Applicant requests a modification of the restriction requirement which omits claim 192 from the proposed election because the binding partner in the claim is one that inactivates or renders TSH receptors unresponsive, which is different from the binding partner of amended claim 121 (Remarks, p. 19 of 19, fourth paragraph). Applicant's arguments and request for reconsideration have been fully considered, and they are persuasive in part.

Applicant's request to rejoin Groups I and II, the antibody binding partner and polynucleotide are not persuasive. Applicant's argument that "[a]s a general rule, PCT Unity of Invention Rules do not

separate nucleotide and corresponding amino acid sequences in different inventions" (Remarks, p. 18 of 19, fifth paragraph) is without basis in fact or at law. A general rule requiring the co-extensive examination of antibody claims and polynucleotide claims does not exist under PCT Unity of Invention Rules (see MPEP 1850). The inventions of Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features. The antibody binding partners of Group I remain anticipated under WO 91/09137 (27 June 1991) even in light of Applicant's claim amendments.

Applicant's amendment to claim 121, for example, does not further limit the anticipation of WO 91/09137 over claim 121 because the addition of the phrase "wherein the binding partner has a characteristic of patient serum TSH receptor autoantibodies" is not sufficient to further limit the claim. Applicant has not set forth any limiting characteristics that distinguish the antibodies of claim 121 over the antibodies of the cited art. The generic phrase "a characteristic" in line 7 of claim 121 could be any structural or functional characteristic. Because Applicant has not recited any defining or distinguishable characteristics of patient serum TSH receptor autoantibodies in claim 121 that would permit the antibodies of claim 121 to be distinguished over the TSH receptor monoclonal antibodies of the prior art, any characteristic of patient serum TSH receptor autoantibodies will suffice, including simply that they bind TSH receptors.

Additionally, Applicant's argument that "there is no mention of autoantibodies as found in patient serum" in the WO 91/09137 reference, is without merit (Remarks, p. 18 of 19, third paragraph). Applicant is specifically directed to Example VIII (pp. 101-113), which teaches the use of the anti-TSHR monoclonal antibodies in competitive binding assays with TSH (see also p. 101, lines 7-33). Example VIII discusses autoantibodies in the serum of patients with autoimmune thyroid disease. The characteristics of those autoantibodies include interacting with the TSHR and competing with TSH for binding to TSHR, as well as stimulating TSHR antibodies that induce cAMP production in thyroid cells. Example VIII also recites that both types of autoantibodies (competitive and stimulatory TSHR binding antibodies) may be present in the same patient (p. 101, lines 31-32). WO 91/09137 also teaches that the anti-TSHR monoclonal antibodies taught therein may be used in competitive binding assays, thus clearly demonstrating that the antibodies taught by WO 91/09137 have the functional a characteristic of competitive binding with naturally occurring autoantibodies against the TSHR (compare instant claim 1). Because WO 91/09137 teaches binding partners for a TSH receptor comprising antibodies, including monoclonal antibodies (pages 36-42, especially p. 39), the remaining claims lack the same or

corresponding special technical feature because the anti-TSHR monoclonal antibodies of claim 121 do not make a contribution over the prior art.

However, after carefully considering Applicant's request to re-restrict claim 192 away from Group I based on the reasoning that the binding partner in claim 192 is one that inactivates or renders TSH receptors unresponsive, which is different from the binding partner of amended claim 121 (Remarks, p. 19 of 19, fourth paragraph), the lack of unity Restriction Requirement has been fully reconsidered. **Accordingly, the previous Requirement for Restriction/Election is WITHDRAWN and a new Requirement for Restriction/Election, based on the same anticipatory reference, is made.**

2. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 121, 122, 125,-137, drawn to a binding partner for a TSH receptor comprising or derived from an antibody reactive with a TSH receptor.

Group II, claim(s) 138-139, 141-143, 145-146 drawn to a binding partner for a TSH receptor that competes for binding with a TSHR with the binding partner of claim 121.

Group III, claim(s) 189-191, drawn to a combination of a binding partner for a TSH receptor and an agent different from the binding partner and capable of stimulating a TSH receptor.

Group IV, claim(s) 192, drawn to a combination of a binding partner for a TSH receptor and an agent capable of inactivating a TSH receptor.

Group V, claim(s) 147-155, drawn to a polynucleotide.

Group VI, claim(s) 156-167, and 195-196, drawn to a method of making a binding partner.

Group VII, claim(s) 168-172, drawn to a method of screening autoantibodies.

Group VIII, claim(s) 173-174, drawn to a method of assaying and evaluating TSH binding partners or ligands.

Group IX, claim(s) 175-176, drawn to a method of identifying epitopes.

Group X, claim(s) 177-178, drawn to anti-idiotype antibodies.

Group XI, claim(s) 179-183, 187-188, drawn to a method for treating an autoimmune disease.

Group XII, claim(s) 184-186, drawn to a method for stimulating thyroid or other tissue containing

the TSH receptor.

Group XIII, claim(s) 193-194, drawn to a method of using a binding partner as a replacement source for patient serum or plasma.

The inventions listed as Groups I-XIII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: claim 1 is anticipated by WO 91/09137 (27 June 1991) (cited in Applicant's IDS of 20 July 2005). WO 91/09137 teaches binding partners for a TSH receptor comprising antibodies, including monoclonal antibodies (pages 36-42, especially p. 39). Example VIII (pp. 101-113), teaches the use of the anti-TSHR monoclonal antibodies in competitive binding assays with TSH (see especially p. 101, lines 7-33). Example VIII discusses autoantibodies in the serum of patients with autoimmune thyroid disease. The characteristics of those autoantibodies include interacting with the TSHR and competing with TSH for binding to TSHR, as well as stimulating TSHR antibodies that induce cAMP production in thyroid cells. Example VIII also recites that both types of autoantibodies (competitive and stimulatory TSHR binding antibodies) may be present in the same patient (p. 101, lines 31-32). WO 91/09137 also teaches that the anti-TSHR monoclonal antibodies taught therein may be used in competitive binding assays, thus clearly demonstrating that the antibodies taught by WO 91/09137 have the functional a characteristic of competitive binding with naturally occurring autoantibodies against the TSHR (compare instant claim 1). Because WO 91/09137 teaches binding partners for a TSH receptor comprising antibodies, including monoclonal antibodies (pages 36-42, especially p. 39), the remaining claims lack the same or corresponding special technical feature. WO 91/09137 teaches all of the limitations of original claim 1. Because WO 91/09137 teaches anti-TSHR monoclonal antibodies that meet all of the limitations of claim 121, the binding compositions of Group II, the combination binding compositions of Groups III and IV, the polynucleotides of Group V, the methods of Groups VI-IX and XI-XIII, and the anti-idiotype antibodies of Group X lack the same or a corresponding special technical feature that makes a contribution over the prior art. Because the remaining claims lack the same or corresponding special technical feature, restriction is required. See 37 CFR 1.475 and MPEP 1850.

3. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1 and as such, the species are **RESTRICTED.** The SEQ ID NOs recited below are drawn to unique and distinct sequences which have different structures and functions and do not have a common core structure and common activity.

The species are as follows:

SEQ ID NOs: 1, 2, 3, 4, 6, 7, 8, 9, 10, 11, 12, 13, 15, 16, 17, 18, 19, 20, 21, 22, 24, 25, 26, 27, 29, 20, 31, 32, 34, 35, 36, 37.

Applicant is required, in reply to this action, to elect **a single species** to which the claims **shall be restricted**. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

4. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

5. Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point

out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

6. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

7. It is also noted that the status identifier for claim 121 is incorrect in Applicant's response, filed 23 October 2007. Normally, an incorrect status identifier would be held as non-responsive. However, in order to promote compact prosecution and clarify all of the outstanding issue regarding the lack of unity restriction requirement, Applicant is requested to correct the status identifier in response to this action. It is also noted that Applicant has indicated claims as withdrawn. Applicant may not sua sponte indicate that claims are withdrawn. The examiner designates that claims are withdrawn. Applicant may then indicated withdrawn claims in the status identifier in response to an Office Action from an examiner.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cherie M. Woodward whose telephone number is (571) 272-3329. The examiner can normally be reached on Monday - Friday 9:00am-5:30pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-

direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Cherie M. Woodward/
Examiner, Art Unit 1647